Abstract

Introduction: Tacrolimus is used as an immunosuppressive drug for patients undergo to organ transplants surgeries or suffered from inflammatory skin diseases. Oral administration of tacrolimus has some limitations, including hepatic first-pass metabolism, very low solubility, secretion from the gastrointestinal tract via P-glycoproteins. In this study, NLC nanoparticles were used to overcome these limitations. Lipid nanoparticles may improve the absorption of substances in the gastrointestinal tract, prevent chemical and enzymatic degradation of the loaded drug, as well as reduce the side effects and toxicity of the drug delivery system. Also in order to increase the mucoadhesive property of carrier and improve the bioavailability of drug, a chitosan shell was coated on the surface of the NLC nanoparticles.

Materials and Methods: Nanostructured lipid carriers containing drug were prepared by solvent diffusion method. Their particle size was optimized using Design Expert software by central cubic method. The NLCs were coated with chitosan polymer. UV-Vis spectrophotometer was used to analyze the drug concentration in unknown samples. First the absorption calibration diagram was drawn and using it, the concentration of unknown samples was calculated at a wavelength of 245 nm. In addition, the NLC and chitosan-coated NLC nanoparticles were evaluated for physicochemical properties sauch as, determination of entrapment efficiency, drug loading efficiency, Nanoparticle size and zeta potential, thermal analysis, FTIR spectrum, scanning electron microscopy (SEM) imaging and drug release pattern.

Results and Discussion: Design Expert software showed the effect of different parameters on nanoparticle size. According to these analyses, increasing the amount of stearic acid, tween 80 and oleic acid increases the size of nanoparticles and increasing the amount of glyceryl mono stearate decreases the size of nanoparticles. The results also showed that the greatest effect is related to the concentration of stearic acid. The size of optimized NLCs was 98 nm and coating them with chitosan increased their particle size to 166 nm Also the zeta potential for nanoparticles without chitosan coating and with chitosan coating was -27 and 75.8 mV respectively. The drug loading efficiency was 14.69% and the drug Entrapment efficiency was 93%. Interpretation of FTIR spectra and DTA/TGA thermal analysis confirmed the lack of chemical reaction between nanoparticle components as well as the formation of strong hydrogen bonds in the nanoparticle structure. Scanning electron microscopy images showed the spherical shape of the nanoparticles and the coating of chitosan. Comparison of the release pattern of nanoparticles with chitosan coated and uncoated nanoparticles showed that drug release was slower in coated nanoparticles and reaches a steady state with some delay in comparison to NLC.

Keywords: Tacrolimus, nanostructured lipid carrier, Chitosan, Bioavailability, Solvent diffusion, oral drug delivery